TAHC – SEPTEMBER 2005 REPORT

GUIDELINES FOR THE SURVEILLANCE OF FOOT AND MOUTH DISEASE

Article 3.8.7.1.

Introduction

This Appendix defines the principles and provides a guide for the surveillance of foot and mouth disease (FMD) in accordance with Appendix 3.8.1. applicable to countries seeking recognition from the OIE for freedom from FMD, either with or without the use of vaccination. This may be for the entire country or a *zone* ~~or *compartment*~~ within the country. Guidance for countries seeking reestablishment of freedom from FMD for the whole country or a *zone* ~~or a *compartment*~~, either with or without vaccination, following an *outbreak*, as well as guidelines for the maintenance of FMD status are provided. These guidelines are intended to expand on and explain the requirements of Chapter 2.2.10. Applications to the OIE for recognition of freedom should follow the format and answer all the questions posed by the "Questionnaire on FMD" available from the OIE Central Bureau.

The impact and epidemiology of FMD differ widely in different regions of the world and therefore it is impossible to provide specific guidelines for all situations. It is axiomatic that the surveillance strategies employed for demonstrating freedom from FMD at an acceptable level of confidence will need to be adapted to the local situation. For example, the approach to proving freedom from FMD following an *outbreak* caused by a pig-adapted strain of FMD virus (FMDV) should differ significantly from an application designed to prove freedom from FMD for a country or *zone* where African buffaloes (*Syncerus caffer*) provide a potential reservoir of infection. It is incumbent upon the applicant country to submit a dossier to the OIE in support of its application that not only explains the epidemiology of FMD in the region concerned but also demonstrates how all the risk factors are managed. This should include provision of scientifically-based supporting data. There is therefore considerable latitude available to Member Countries to provide a well-reasoned argument to prove that the absence of FMDV infection (in non-vaccinated populations) or circulation (in vaccinated populations) is assured at an acceptable level of confidence.

Surveillance for FMD should be in the form of a continuing programme designed to establish that the whole territory or part of it is free from FMDV infection/circulation.

For the purposes of this Appendix, virus circulation means transmission of FMDV as demonstrated by clinical signs, serological evidence or virus isolation.

Article 3.8.7.2.

General conditions and methods

1. A surveillance system in accordance with Appendix 3.8.1 should be under the responsibility of the *Veterinary Administration*. A procedure should be in place for the rapid collection and transport of samples from suspect cases of FMD to a laboratory for FMD diagnoses as described in the *Terrestrial Manual*.

2. The FMD surveillance programme should:

a) include an early warning system throughout the production, marketing and processing chain for reporting suspicious cases. Farmers and workers who have day-to-day contact with livestock, as well as diagnosticians, should report promptly any suspicion of FMD. They should be supported directly or indirectly (e.g. through private veterinarians or *veterinary para-professionals*) by government information programmes and the *Veterinary Administration*. All suspect cases of FMD should be investigated immediately. Where suspicion cannot be resolved by epidemiological and clinical investigation, samples should be taken and submitted to an *approved laboratory*. This requires that sampling kits and other equipment are available for those responsible for surveillance. Personnel responsible for surveillance should be able to call for assistance from a team with expertise in FMD diagnosis and control;

b) implement, when relevant, regular and frequent clinical inspection and serological testing of high-risk groups of animals, such as those adjacent to an FMD infected country or *zone* (for example, bordering a game park in which infected wildlife are present).

An effective surveillance system will periodically identify suspicious cases that require follow up and investigation to confirm or exclude that the cause of the condition is FMDV. The rate at which such suspicious cases are likely to occur will differ between epidemiological situations and cannot therefore be predicted reliably. Applications for freedom from FMDV infection/circulation should, in consequence, provide details of the occurrence of suspicious cases and how they were investigated and dealt with. This should include the results of laboratory testing and the control measures to which the animals concerned were subjected during the investigation (quarantine, movement stand-still orders, etc.).

Article 3.8.7.3.

Surveillance strategies

1. Introduction

The target population for surveillance aimed at identifying *disease* and *infection* should cover all the susceptible species within the country or *zone* to be recognised as free from FMDV infection/circulation.

The strategy employed may be based on randomised sampling requiring surveillance consistent with demonstrating the absence of FMDV infection/circulation at an acceptable level of statistical confidence. The frequency of sampling should be dependent on the epidemiological situation. Targeted surveillance (e.g. based on the increased likelihood of *infection* in particular localities or species) may be an appropriate strategy. The applicant country should justify the surveillance strategy chosen as adequate to detect the presence of FMDV infection/circulation in accordance with Appendix 3.8.1. and the epidemiological situation. It may, for example, be appropriate to target clinical surveillance at particular species likely to exhibit clear clinical signs (e.g. cattle and pigs). If a Member Country wishes to apply for recognition of a specific *zone* ~~or *compartment*~~ within the country as being free from FMDV infection/circulation, the design of the survey and the basis for the sampling process would need to be aimed at the population within the *zone* ~~or *compartment*~~.

For random surveys, the design of the sampling strategy will need to incorporate an epidemiologically appropriate design prevalence. The sample size selected for testing will need to be large enough to detect infection/circulation if it were to occur at a predetermined minimum rate. The sample size and expected disease prevalence determine the level of confidence in the results of the survey. The applicant country must justify the choice of design

prevalence and confidence level based on the objectives of surveillance and the epidemiological situation, in accordance with Appendix 3.8.1. Selection of the design prevalence in particular clearly needs to be based on the prevailing or historical epidemiological situation.

Irrespective of the survey design selected, the sensitivity and specificity of the diagnostic tests employed are key factors in the design, sample size determination and interpretation of the results obtained. Ideally, the sensitivity and specificity of the tests used should be validated for the vaccination/infection history and production class of animals in the target population.

Irrespective of the testing system employed, surveillance design should anticipate the occurrence of false positive reactions. If the characteristics of the testing system are known, the rate at which these false positives are likely to occur can be calculated in advance. There needs to be an effective procedure for following up positives to ultimately determine with a high level of confidence, whether they are indicative of infection/circulation or not. This should involve both supplementary tests and follow-up investigation to collect diagnostic material from the original sampling unit as well as herds which may be epidemiologically linked to it.

The principles involved in surveillance for *disease/infection* are technically well defined. The design of surveillance programmes to prove the absence of FMDV infection/circulation needs to be carefully followed to avoid producing results that are either insufficiently reliable to be accepted by the OIE or international trading partners, or excessively costly and logistically complicated. The design of any surveillance programme, therefore, requires inputs from professionals competent and experienced in this field.

2. Clinical surveillance

Clinical surveillance aims at detecting clinical signs of FMD by close physical examination of susceptible animals. Whereas significant emphasis is placed on the diagnostic value of mass serological screening, surveillance based on clinical inspection should not be underrated. It may be able to provide a high level of confidence of detection of disease if a sufficiently large number of clinically susceptible animals is examined.

Clinical surveillance and laboratory testing should always be applied in series to clarify the status of FMD suspects detected by either of these complementary diagnostic approaches. Laboratory testing may confirm clinical suspicion, while clinical surveillance may contribute to confirmation of positive serology. Any sampling unit within which suspicious animals are detected should be classified as infected until contrary evidence is produced.

A number of issues must be considered in clinical surveillance for FMD. The often underestimated labour intensity and the logistical difficulties involved in conducting clinical examinations should not be underestimated and should be taken into account.

Identification of clinical cases is fundamental to FMD surveillance. Establishment of the molecular, antigenic and other biological characteristics of the causative virus, as well as its source, is dependent upon disclosure of such animals. It is essential that FMDV isolates are sent regularly to the regional reference laboratory for genetic and antigenic characterization.

3. Virological surveillance

Virological surveillance using tests described in the *Terrestrial Manual* should be conducted:

a) to monitor at risk populations;

b) to confirm clinically suspect cases;

c) to follow up positive serological results;

d) to test "normal" daily mortality, to ensure early detection of infection in the face of vaccination or in *establishments* epidemiologically linked to an *outbreak*.

4. Serological surveillance

Serological surveillance aims at detecting antibodies against FMDV. Positive FMDV antibody test results can have four possible causes:

a) natural infection with FMDV;

b) vaccination against FMD;

c) maternal antibodies derived from an immune dam (maternal antibodies in cattle are usually found only up to 6 months of age but in some individuals and in some species, maternal antibodies can be detected for considerably longer periods);

d) heterophile (cross) reactions.

It is important that serological tests, where applicable, contain antigens appropriate for detecting antibodies against viral variants (types, subtypes, lineages, topotypes, etc.) that have recently occurred in the region concerned. Where the probable identity of FMDVs is unknown or where exotic viruses are suspected to be present, tests able to detect representatives of all serotypes should be employed (e.g. tests based on nonstructural viral proteins – see below).

It may be possible to use serum collected for other survey purposes for FMD surveillance. However, the principles of survey design described in this Appendix and the requirement for a statistically valid survey for the presence of FMDV should not be compromised.

The discovery of clustering of seropositive reactions should be foreseen. It may reflect any of a series of events, including but not limited to the demographics of the population sampled, vaccinal exposure or the presence of field strain infection. As clustering may signal field strain infection, the investigation of all instances must be incorporated in the survey design. If vaccination cannot be excluded as the cause of positive serological reactions, diagnostic methods should be employed that detect the presence of antibodies to nonstructural proteins (NSPs) of FMDVs as described in the *Terrestrial Manual*.

The results of random or targeted serological surveys are important in providing reliable evidence that FMDV infection is not present in a country or *zone*. It is therefore essential that the survey be thoroughly documented.

Article 3.8.7.4.

Countries applying for freedom from FMD for the whole country or a zone ~~or a compartment~~ where vaccination is not practised

In addition to the general conditions described in Chapter 2.2.10., a Member Country applying for recognition of FMD freedom for the country or a *zone* ~~or a *compartment*~~ where vaccination is not practised should provide evidence for the existence of an effective surveillance programme. The strategy and design of the surveillance programme will depend on the prevailing epidemiological circumstances and will be planned and implemented according to general conditions and methods in

this Appendix, to demonstrate absence of FMDV infection, during the preceding 12 months in susceptible populations. This requires the support of a national or other laboratory able to undertake identification of FMDV infection through virus/antigen/genome detection and antibody tests described in the *Terrestrial Manual*.

Article 3.8.7.5.

Countries~~,~~ or zones ~~or compartments~~ applying for freedom from FMD where vaccination is practised

In addition to the general conditions described in Chapter 2.2.10., a Member Country applying for recognition of country or *zone* ~~or compartment~~ freedom from FMD with vaccination should show evidence of an effective surveillance programme planned and implemented according to general conditions and methods in this Appendix. Absence of clinical disease in the country~~,~~ or *zone* ~~or compartment~~ for the past 2 years should be demonstrated. Furthermore, surveillance should demonstrate that FMDV has not been circulating in any susceptible population during the past 12 months. This will require serological surveillance incorporating tests able to detect antibodies to NSPs as described in the *Terrestrial Manual*. Vaccination to prevent the transmission of FMDV may be part of a disease control programme. The level of herd immunity required to prevent transmission will depend on the size, composition (e.g. species) and density of the susceptible population. It is therefore impossible to be prescriptive. However, the aim should, in general, be to vaccinate at least 80% of the susceptible population. The vaccine must comply with the *Terrestrial Manual*. Based on the epidemiology of FMD in the country~~,~~ or *zone* ~~or compartment~~, it may be that a decision is reached to vaccinate only certain species or other subsets of the total susceptible population. In that case, the rationale should be contained within the dossier accompanying the application to the OIE for recognition of status.

Evidence to show the effectiveness of the vaccination programme should be provided.

Article 3.8.7.6.

Countries~~,~~ or zones ~~or compartments~~ re-applying for freedom from FMD where vaccination is either practised or not practised, following an outbreak

In addition to the general conditions described in Chapter 2.2.10., a country re-applying for country~~,~~ or *zone* ~~or compartment~~ freedom from FMD where vaccination is practised or not practised should show evidence of an active surveillance programme for FMD as well as absence of FMDV infection/circulation. This will require serological surveillance incorporating, in the case of a country~~,~~ or *zone* ~~or compartment~~ practising vaccination, tests able to detect antibodies to NSPs as described in the *Terrestrial Manual*.

Four strategies are recognised by the OIE in a programme to eradicate FMDV infection following an *outbreak*:

1. slaughter of all clinically affected and in-contact susceptible animals;

2. slaughter of all clinically affected and in-contact susceptible animals and vaccination of at-risk animals, with subsequent slaughter of vaccinated animals;

3. slaughter of all clinically affected and in-contact susceptible animals and vaccination of at-risk

animals, without subsequent slaughter of vaccinated animals;

4. vaccination used without slaughter of affected animals or subsequent slaughter of vaccinated animals.

The time periods before which an application can be made for re-instatement of freedom from FMD depends on which of these alternatives is followed. The time periods are prescribed in Article 2.2.10.7.

In all circumstances, a Member Country re-applying for country~~,~~ or *zone* ~~*or compartment*~~ freedom from FMD with vaccination or without vaccination should report the results of an active surveillance programme implemented according to general conditions and methods in this Appendix.

Article 3.8.7.7.

The use and interpretation of serological tests (see Figure 1)

The recommended serological tests for FMD surveillance are described in the *Terrestrial Manual.*

Animals infected with FMDV produce antibodies to both the structural proteins (SP) and the nonstructural proteins (NSP) of the virus. Tests for SP antibodies to include SP-ELISAs and the virus neutralisation test (VNT). The SP tests are serotype specific and for optimal sensitivity should utilise an antigen or virus closely related to the field strain against which antibodies are being sought. Tests for NSP antibodies include NSP I-ELISA 3ABC and the electro-immunotransfer blotting technique (EITB) as recommended in the *Terrestrial Manual* or equivalent validated tests. In contrast to SP tests, NSP tests can detect antibodies to all serotypes of FMD virus. Animals vaccinated and subsequently infected with FMD virus develop antibodies to NSPs, but in some, the titre may be lower than that found in infected animals that have not been vaccinated. Both the NSP I-ELISA 3ABC and EITB tests have been extensively used in cattle. Validation in other species is ongoing. Vaccines used should comply with the standards of the *Terrestrial Manual* insofar as purity is concerned to avoid interference with NSP antibody testing.

Serological testing is a suitable tool for FMD surveillance. The choice of a serosurveillance system will depend on, amongst other things, the vaccination status of the country. A country, which is free from FMD without vaccination, may choose serosurveillance of high-risk subpopulations (e.g. based on geographical risk for exposure to FMDV). SP tests may be used in such situations for screening sera for evidence of FMDV infection/circulation if a particular virus of serious threat has been identified and is well characterised. In other cases, NSP testing is recommended in order to cover a broader range of strains and even serotypes. In both cases, serological testing can provide additional support to clinical surveillance. Regardless of whether SP or NSP tests are used in countries that do not vaccinate, a diagnostic follow-up protocol should be in place to resolve any presumptive positive serological test results.

In areas where animals have been vaccinated, SP antibody tests may be used to monitor the serological response to the vaccination. However, NSP antibody tests should be used to monitor for FMDV infection/circulation. NSP-ELISAs may be used for screening sera for evidence of infection/circulation irrespective of the vaccination status of the animal. All herds with seropositive reactors should be investigated. Epidemiological and supplementary laboratory investigation results should document the status of FMDV infection/circulation for each positive herd. Tests used for

confirmation should be of high diagnostic specificity to eliminate as many false positive screening test reactors as possible. The diagnostic sensitivity of the confirmatory test should approach that of the screening test. The EITB or another OIE-accepted test should be used for confirmation.

Information should be provided on the protocols, reagents, performance characteristics and validation of all tests used.

1. <u>The follow-up procedure in case of positive test results if no vaccination is used in order to establish or re-establish FMD free status without vaccination</u>

Any positive test result (regardless of whether SP or NSP tests were used) should be followed up immediately using appropriate clinical, epidemiological, serological and, where possible, virological investigations of the reactor animal at hand, of susceptible animals of the same epidemiological unit and of susceptible animals that have been in contact or otherwise epidemiologically associated with the reactor animal. If the follow up investigations provide no evidence for FMDV infection, the reactor animal shall be classified as FMD negative. In all other cases, including the absence of such follow-up investigations, the reactor animal should be classified as FMD positive.

2. <u>The follow-up procedure in case of positive test results if vaccination is used in order to establish or re-establish FMD free status with vaccination</u>

In case of vaccinated populations one has to exclude that positive test results are indicative of virus circulation. To this end the following procedure should be followed in the investigation of positive serological test results derived from surveillance conducted on FMD vaccinated populations.

The investigation should examine all evidence that might confirm or refute the hypothesis that the positive results to the serological tests employed in the initial survey were not due to virus circulation. All the epidemiological information should be substantiated and the results should be collated in the final report.

It is suggested that in the primary sampling units where at least one animal reacts positive to the NSP test, the following strategy(ies) should be applied:

a) Following clinical examination, a second serum sample should be taken from the animals tested in the initial survey after an adequate interval of time has lapsed, on the condition that they are individually identified, accessible and have not been vaccinated during this period. Antibody titres against NSP at the time of retest should be statistically either equal to or lower than those observed in the initial test if virus is not circulating.

   The animals sampled should remain in the holding pending test results and should be clearly identifiable. If the three conditions for retesting mentioned above cannot be met, a new serological survey should be carried out in the holding after an adequate period of time, repeating the application of the primary survey design and ensuring that all animals tested are individually identified. These animals should remain in the holding and should not be vaccinated, so that they can be retested after an adequate period of time.

b) Following clinical examination, serum samples should be collected from representative numbers of cattle that were in physical contact with the primary sampling unit. The magnitude and prevalence of antibody reactivity observed should not differ in a statistically significant manner from that of the primary sample if virus is not circulating.

c) Following clinical examination, epidemiologically linked herds should be serologically tested and satisfactory results should be achieved if virus is not circulating.

d) Sentinel animals can also be used. These can be young, unvaccinated animals or animals in which maternally conferred immunity has lapsed and belonging to the same species resident within the positive initial sampling units. They should be serologically negative if virus is not circulating. If other susceptible, unvaccinated ruminants (sheep, goats) are present, they could act as sentinels to provide additional serological evidence.

Laboratory results should be examined in the context of the epidemiological situation. Corollary information needed to complement the serological survey and assess the possibility of viral circulation includes but is not limited to:

– characterization of the existing production systems;

– results of clinical surveillance of the suspects and their cohorts;

– quantification of vaccinations performed on the affected sites;

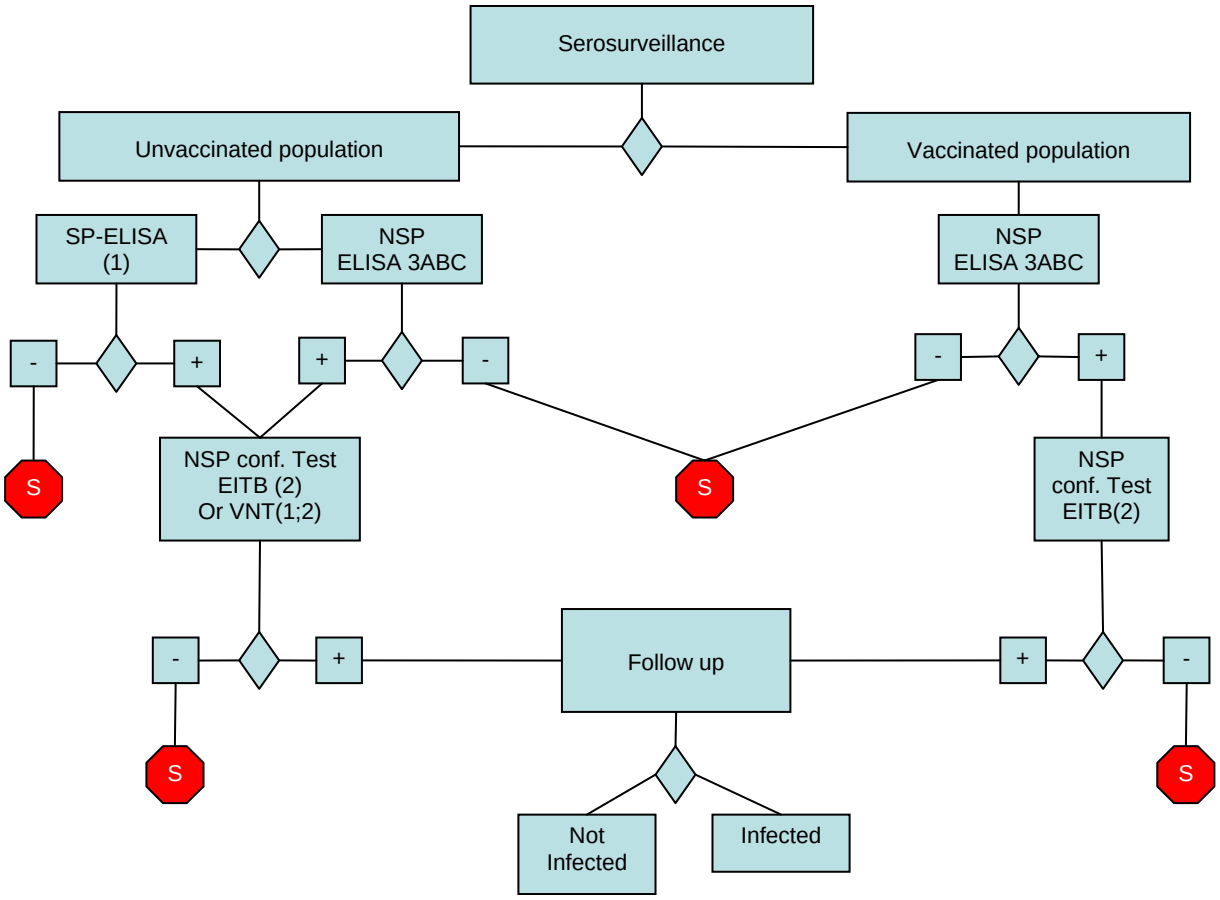
– sanitary protocol and history of the *establishments* with positive reactors;

– control of animal identification and movements;

– other parameters of regional significance in historic FMDV transmission.

The entire investigative process should be documented as standard operating procedure within the surveillance programme.

Figure 1 ***Schematic representation of laboratory tests for determining evidence of FMDV infection through or following serological surveys***



Key:

ELISA	Enzyme-linked immunosorbent assay
VNT	Virus neutralisation test
NSP	Nonstructural protein(s) of foot and mouth disease virus (FMDV)
3ABC	NSP antibody test
EITB	Electro-immuno transfer blotting technique (Western blot for NSP antibodies of FMDV)
~~OP~~	~~Oesophageal–pharyngeal sample~~
SP	Structural protein test
S	No evidence of FMDV